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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,436	12/22/2004	Hilde Azjin	026038.0248PTUS	7541

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
05/11/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,436	AZJIN ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 2 February 2010.

Claims 1-4 and 6-10 have been cancelled.

Claim 5 has been amended. New claim 11 has been added.

Claims 5 and 11 are pending and currently examined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(Prior Rejection – Withdrawn) The rejection of claim 5 under 35 U.S.C. §103(a) as being obvious over Stein *et al.* (1994, hereinafter "Stein") in view of Servais *et al.* (10 March 2001, GenBank Accession Number CAB86592, GI:7529531, hereinafter "Servais") and Kim *et al.* (2001, hereinafter "Kim") **is withdrawn** in response to Applicants' amendment.

Response to Arguments

Applicant's arguments with respect to claim 5 have been considered but are moot in view of the new ground of rejection.

(New Rejection – Necessitated by Amendment) Claims 5 and 11 are rejected under 35 U.S.C. §103(a) as being obvious over Stein *et al.* (1994, hereinafter "Stein") in view of Bacheler *et al.* (2001, hereinafter "Bacheler") and as evidenced by Servais *et al.* (10 March 2001, GenBank Accession Number CAB86592, GI:7529531, hereinafter "Servais").

The instant claim is directed to a method for evaluating a change in susceptibility of HIV to a reverse transcriptase inhibitor (RTI) for a second anti-HIV therapy comprising:

(i) receiving a sample from an HIV-infected patient who has been treated with a first anti-HIV therapy;

(ii) determining whether said sample from said HIV-infected patient comprises an HIV reverse transcriptase having a mutation at the position 194 from the wild type amino acid glutamate to glycine (E194G) as compared to the wild-type HIV strain IIIB/LAI;

(iii) introducing a RTI selected from a group including Nevirapine, Efavirenz and Delavirdine for said second anti-HIV therapy to said sample from said HIV-infected patient containing said mutation;

(iv) determining the susceptibility of said HIV having said reverse transcriptase mutation of step (ii) to said RTI in said sample;

(v) comparing the anti-HIV drug effectiveness in said sample containing said reverse transcriptase mutation with a sample not containing such said mutation; and

(vi) correlating the presence of said reverse transcriptase mutation of step (ii) to a change in the susceptibility of said RTI.

(vii) determining whether said sample from said HIV-infected patient comprises an HIV reverse transcriptase having a mutation E194G and at least one additional mutation at the position selected from 41, 62, 65, 67, 69, 70, 74, 75, 98, 100, 101,103, 106, 108, 116, 118, 138, 151, 178, 181, 184, 188, 190, 210, 215, 219, 225, 227, 230, 234, 236, and 238 compared to the wild-type HIV strain IIIB/LAI;

(viii) determining the susceptibility of said HIV having said reverse transcriptase mutations of step (vii) to said HIV reverse transcriptase inhibitor in said sample;

(ix) comparing the anti-HIV drug effectiveness in said sample containing said reverse transcriptase mutations with a sample not containing such said mutations; and

(x) correlating the presence of said reverse transcriptase mutations of step (vii) to a change in the susceptibility of said HIV reverse transcriptase inhibitor

Stein discloses the claimed step (i) receiving a sample from an HIV-infected patient, and step (ii) determining whether the sample comprises a nucleic acid encoding HIV reverse transcriptase having a mutation at position 194 from wild type amino acid glutamate (Glu or E) (page 216, Table I); and correlating the presence of the mutation to a change in effectiveness or susceptibility of a nucleoside reverse transcriptase inhibitor (RTI), azidothymidine (AZT) (page 117 and Table II).

Stein is silent on the specific mutant amino acid at position 194 (E194G). However, according to the GenBank sequence G1:7529531, Servais evidences the E194G mutation in the reverse transcriptase in samples from patients who have been treated with a first anti-HIV therapy containing RTIs zidovudine and zalcitabine.

Stein does not expressly suggest introducing an RTI as a second therapy to a pre-treated patient sample containing drug-resistant mutation(s).

Bacheler discloses a method comprising the following steps: step (i) receiving a sample from an HIV-infected patient who has been treated with a first anti-HIV therapy of efavirenz/indinavir combination regimen, step (ii) determining HIV RT mutations in the sample by genotypic characterization, an in vitro drug susceptibility assay which is the same as step (iii) introducing an RTI, Efavirenz, Nevirapine, or Delavirdine, in a second therapy to the sample from the HIV-infected pre-treated patient, step (iv) determining the susceptibility of the HIV isolate to the HIV RTI in the sample, step (v) comparing the anti-HIV drug effectiveness in the sample with a wild type HIV HXB2, step (vi) correlating the presence of RT mutation(s) to a change in the susceptibility of the HIV RTI by summarizing the results of the in vitro susceptibility tests and the corresponding viral genotypes in a table, step (vii) determining whether the sample comprises an HIV RT mutation at position 41, 67, 70, 74, 98, 100, 101, 103, 106, 108, 181, 184, 188, 190, 215, 225 or 227, and analyzing drug susceptibility as in step (viii)-(x). See page 5000, right column, last paragraph; and page 5002-5003, TABLE 1.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify evaluation method of Stein to further include the steps for evaluating a second therapy RTI as suggested by Bacheler. One having ordinary skill in the art would have been motivated to do this so that the E194G mutation contributes to a more complete and accurate drug evaluation for any novel HIV RTIs while the in vitro test of introducing a RTI to a pre-treated patient sample containing the known RTI-resistant mutation(s), as a result of the first anti-HIV therapy, helps identify more potent RTIs in a rapid assay. There would have been a reasonable expectation of success because the steps of evaluating a change in susceptibility of an HIV isolate to any given inhibitor is well established in the art as disclosed by Bacheler and since Stein already identified a mutation at position 194 in the HIV RT and correlated it with resistance to an RTI such as AZT and given that E194G mutation is already known in the art as evidenced by Servais. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645